

Identification of substandard and counterfeit antimalarial pharmaceuticals chloroquine, doxycycline, and primaquine using surface-enhanced Raman scattering

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Supporting Information

Figure S1: Representative TEM images of the silver nanoparticles used in SERS analysis

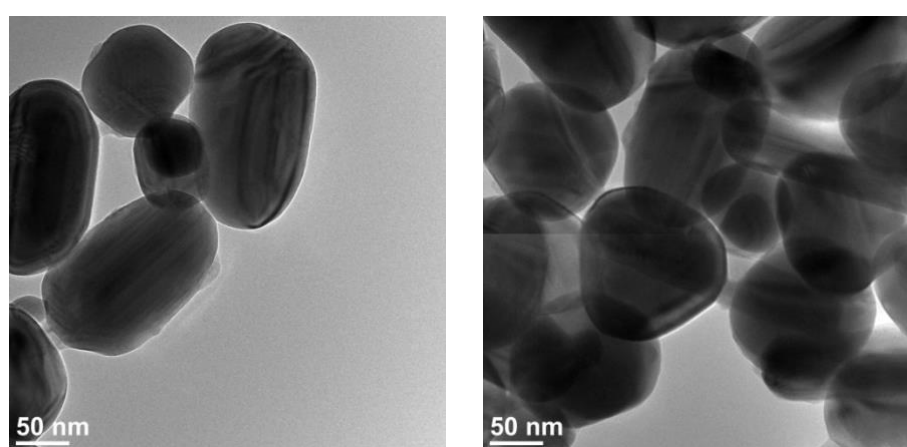


Table S1: Active pharmaceutical ingredient (API) content of unknown red team samples

Sample	Excipient	Excipient Content	API Content (% of Label Claim)
Chloroquine 1	N/A	N/A	100%
Chloroquine 2	Acetaminophen	100%	0%
Chloroquine 3	Starch	52%	48%
Chloroquine 4	N/A	0%	100%
Doxycycline 1	N/A	0%	100%
Doxycycline 2	N/A	0%	100%
Doxycycline 3	Starch	100%	0%
Doxycycline 4	Acetaminophen	50%	50%
Primaquine A	Acetaminophen	100%	0%
Primaquine B	N/A	0%	100%
Primaquine C	N/A	0%	100%
Primaquine D	Starch	50%	50%
Primaquine E	Rifampicin	100%	0%

Table S2: Raman/SERS peak assignments for 4-mercaptobenzoic acid (4-MBA), chloroquine, and doxycycline

	Shift (cm ⁻¹)	Mode Assignment
4-MBA	1076	$\nu(\text{C-C})$ stretch
4-MBA	1132	$\delta(\text{C-H})$
4-MBA	1173	$\delta(\text{C-H})$
4-MBA	1357	$\nu(\text{COO}^-)$
4-MBA	1585	$\nu(\text{C-C})$ stretch
Chloroquine	595	$\Delta(\text{quin.}, \text{C-Cl})$
Chloroquine	757	$\Delta(\text{N-H})$, quin. deformations, $\nu(\text{C-Cl})$, $\delta(\text{N-H})$
Chloroquine	1102	$\nu(\text{Cl-quin.})$
Chloroquine	1161	$\nu(\text{C-C})$
Chloroquine	1373	$\nu(\text{C-C})$ quin., $\delta(\text{C-H})$ quin., $\delta(\text{C-CH}_3)$
Chloroquine	1385	$\nu(\text{C-C})$ benzene
Chloroquine	1406	$\nu(\text{C-C})$, $\delta(\text{C-H})$ ring
Chloroquine	1452	$\nu(\text{C-C})$, $\delta(\text{C-H})$
Chloroquine	1476	$\nu(\text{C-C})$ ring
Chloroquine	1555	$\nu(\text{C=N})$ ring
Chloroquine	1612	$\nu(\text{C=N})$, $\delta(\text{N-H})$
Chloroquine	1637	$\Delta(\text{N-H})$
Doxycycline	1160	$\delta(\text{C-H})$
Doxycycline	1279	$\nu(\text{C-C})$
Doxycycline	1333	$\nu(\text{C-C})$
Doxycycline	1609	$\nu(\text{C-C})$

Figure S2: Matlab script for obtaining correlation coefficient and peak-area ratio analysis

For Correlation

```
% import data first
BSubData= msbackadj(x,RawData)           % BSubData is the Raw Data after Baseline
Subtraction
Correlation = corr(BSubData,Reference)    % Yields correlation coefficient between unknown
                                         samples and reference spectra
```

For peak-area-ratio

```
% import data first
For n = 1:numfiles
    Range1=1205:1255;
    Range2=305:345;
    Peakarea1(n)=trapz(BSubData(range1,n)); %Integrates reference band
    Peakarea2(n)=trapz(BSubData(range2,n)); % Integrates API Band
    Peakarea1./Peakarea2
```

End

% Ans variable contains peak-area-ratio values of all unknown spectra (1 through n).

Table S3: Correlation coefficient and peak-area ratio analysis - red team study results

DOXYCYCLINE	Sample	Correlation Coefficient	API Content
	Doxycycline 1	0.962	Present
		0.975	
		0.971	
	Doxycycline 2	0.946	Present
		0.943	
		0.939	
	Doxycycline 3	0.59	Absent
		0.59	
		0.599	
	Doxycycline 4	0.874	Present
		0.895	
		0.809	
	Reference Ratio Values	Lower Limit	Upper Limit
		0.9	1.9
	Sample	Ratio	Quality
	Doxycycline 1	1.3	Good
	Doxycycline 2	0.9	Good
	Doxycycline 4	0.8	Bad

PRIMAQUINE	Sample	Correlation Coefficient	API Content
	Primaquine 1	0.413475	Absent
		0.405734	
		0.435432	
	Primaquine 2	0.997577	Present
		0.997542	
		0.997212	
	Primaquine 3	0.997387	Present
		0.996841	
		0.997385	
	Primaquine 4	0.584478	Present
		0.997049	
		0.994303	
	Primaquine 5	0.378954	Absent
		0.379498	
		0.584478	
	Reference Ratio Values	Lower Limit	Upper Limit
		5.1	5.3
	Sample	Ratio	Quality
	Primaquine 2	5.2	Good
	Primaquine 3	5.2	Good
	Primaquine 4	5.5	Bad
CHLOROQUINE	Sample	Correlation Coefficient	API Content
	Chloroquine 1	0.953202	Present
		0.957486	
		0.958909	
	Chloroquine 2	0.517055	Absent
		0.480542	
		0.431983	
	Chloroquine 3	0.946333	Present
		0.950234	
		0.956246	
	Chloroquine 4	0.956934	Present
		0.953933	
		0.947799	
	Reference Ratio Values	Lower Limit	Upper Limit
		0.8	1.0
	Sample	Ratio	Quality
	Chloroquine 1	0.8	Good
	Chloroquine 3	1.3	Bad
	Chloroquine 4	1.0	Good

Figure S3: Pure 4-mercaptobenzoic acid (4-MBA) SERS spectrum

